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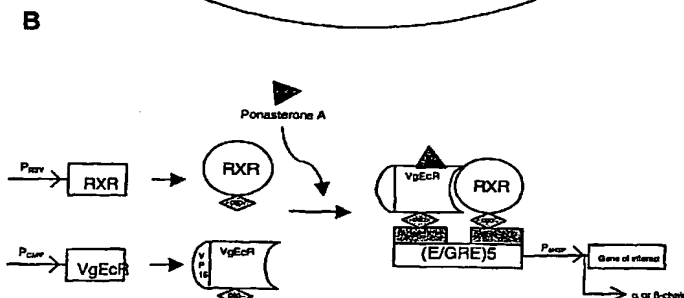
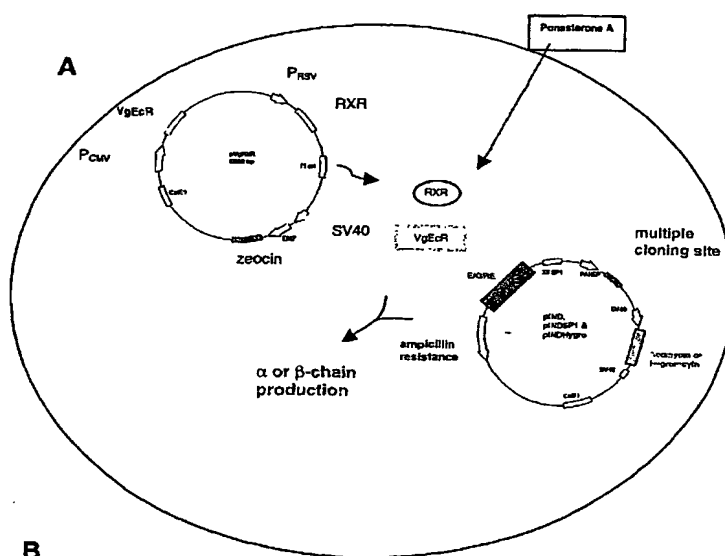
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[Continued on next page]

(54) Title: RECOMBINANT CELL LINE



(57) Abstract: The invention relates to a recombinant cell line capable of inducible expression of an α and/or β subunit of interleukin 12 (IL-12), and an ecdosymeinducible expression vector capable of transfecting a host cell to produce the recombinant cell line of the invention. The invention also relates to a method of screening a candidate compound for the ability to inhibit IL-12 formation and secretion which comprises the steps of incubating a cell line according to the invention with the candidate compound. The invention also relates to the use of the CELEBREX-type of compounds as inhibitors.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

ational Application No

03/06404

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/19 A61K31/415

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DUNLOP ET AL: "Inducible expression and pharmacology of the human excitatory amino acid transporter 2 subtype of L-glutamate transporter" BRITISH JOURNAL OF PHARMACOLOGY, vol. 128, 1999, pages 1485-1490, XP002286498 * See Abstract (1,2,7) and page 1487 (Results / Inducible expression) *	1-10,12, 14-23, 26,28-30
Y	GRAHAM ET AL: "Ecdysone-controlled expression of transgenes" EXPERT OPINION ON BIOLOGICAL THERAPY, vol. 2, June 2002 (2002-06), pages 525-535, XP008032350 * See pages 525-530 (Sections 1 and 2) *	1-10,12, 14-23, 26,28-30
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *8* document member of the same patent family

Date of the actual completion of the international search

8 July 2004

Date of mailing of the international search report

28/07/2004

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INTERNATIONAL SEARCH REPORT

national Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MARTENS ET AL: "Protein disulfide isomerase-mediated cell-free assembly of recombinant interleukin-12 p40 homodimers" EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 267, 2000, pages 6679-6683, XP002286499 * See page 6681 (left column / His6-p40) *	1-10,12, 14-23, 26,28-30
P,Y	NAGY ET AL: "Inducible expression and pharmacology of recombinant NMDA receptors, composed of rat NR1a/NR2B subunits" NEUROCHEMISTRY INTERNATIONAL, vol. 43, July 2003 (2003-07), pages 19-29, XP002286500 * See Abstract *	1-10,12, 14-23, 26,28-30
X	DAVIES ET AL: "Clinical pharmacokinetics and pharmacodynamics of Celecoxib" CLINICAL PHARMACOKINETICS, vol. 38, 2000, pages 225-242, XP008008797 * See page 226 (left column) *	33-41
X	CHEN ET AL: "Selective inhibition of COX-2 is beneficial to mice infected intranasally with VSV" PROSTAGLANDINS AND OTHER LIPID MEDIATORS, vol. 67, February 2002 (2002-02), pages 143-155, XP004344953 * See pages 150-153 (Discussion) *	33-41
X	CUZZOCREA ET AL: "Celecoxib, a selective cyclo-oxygenase-2 inhibitor reduces the severity of experimental colitis induced by dinitrobenzene sulfonic acid in rats" EUROPEAN JOURNAL OF PHARMACOLOGY, vol. 431, 2001, pages 91-102, XP001113036 * See Abstract *	33-41
X	US 2002/119193 A1 (LE ET AL) 29 August 2002 (2002-08-29) * See '0048! / celecoxib, and '0057-0076! / speculative uses against speculative uses *	33-41
A	US 5 972 986 A (SEIBERT ET AL) 26 October 1999 (1999-10-26) cited in the application * See columns 3-4 (Formula I) *	33-41

Continuation of Box I.1

Although Claims 33,35-41 are directed to a method of treatment, the search has been carried out and based on the alleged effects of the compounds.

Note that prior art documents relating to the same compounds for treatment of the same diseases are cited X.

Continuation of Box I.2

Claims Nos.: 31-32

Claims 31-32 relate to undefined inhibitors that may be found by a screening process. These claims are merely desiderata and cannot be searched.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/IB 03/06404

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 31-32
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

03/06404

Patent document
cited in search report

Publication
date

Patent family
member(s)

Publication
date

US 2002119193 A1 29-08-2002 NONE

US 5972986 A 26-10-1999 US 2003220384 A1 27-11-2003
US 2001047024 A1 29-11-2001